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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,142	08/20/2003	Mitsunori Iwamoto	4703/1F214US2	6008
7278	7590	11/18/2005	EXAMINER	
DARBY & DARBY P.C. P. O. BOX 5257 NEW YORK, NY 10150-5257			JOYCE, CATHERINE	
		ART UNIT	PAPER NUMBER	
		1642		

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,142	IWAMOTO ET AL.	
	Examiner Catherine M. Joyce	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 12 October 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 8,11 and 12 is/are pending in the application.
- 4a) Of the above claim(s) 11 and 12 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 8 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

1. Claims 1-7 and 9-10 have been canceled.
2. Claims 8, 11, and 12 are pending, and claims 11 and 12 are withdrawn from consideration as drawn to a non-elected invention
3. Claim 8 is under examination.
4. Applicant's election with traverse of Group I in the reply filed on October 12, 2005 is acknowledged. The traversal is on the ground(s) that searching Groups I and II together would not pose a search burden. This argument is not found persuasive because a search for the polypeptide of Group I would not be coextensive with a search for the antibody of Group II and therefore, a search burden is established. The requirement is still deemed proper and is therefore made FINAL.

Specification

5. The specification on page 1 should be amended to reflect the status of the parent application serial number 09/912,176.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
7. Claim 8 is rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

The claims are drawn to a protein containing an amino acid sequence homologous to the amino acid sequence of SEQ ID NO:1 and having proliferation inhibitory activity on cancer cells or cell death inducing activity.

Although drawn to the DNA arts, the finding in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. v. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that “[a] written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *Id.* At 1567, 43 USPQ2d at 1405. The court also stated that

a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA” without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” *Id.*

Finally, the court addressed the manner by which a genus of cDNAs might be described. “A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.” *Id.*

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that “the written description requirement can be met by ‘show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristicsi.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.’” Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

While the inventions at issue in Lilly and Enzo were DNA constructs, the holdings of those cases are also applicable to claims such as those at issue here wherein a genus of polypeptides is claimed.

Thus, the instant specification may provide an adequate written description of the claimed genus of a protein containing an amino acid sequence homologous to the amino acid sequence of SEQ ID NO:1 and having proliferation inhibitory activity on cancer cells or cell death inducing activity per Lilly by structurally describing a representative number of species within the claimed genus or by describing “structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Alternatively, per Enzo, the specification can show that the claimed invention is complete “by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.”

In this case, the specification does not describe the claimed genus in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any polypeptide in the claimed genus other than SEQ ID NO:1 and one mutant of SEQ ID NO:1 having the claimed activity (i.e. a polypeptide having

amino acids 1-514 of SEQ ID NO:1) (page 40, line 25 to page 41, line 3), nor does the specification provide any partial structure of the claimed genus of polypeptides, nor any physical or chemical characteristics of the claimed genus of polypeptides, nor any functional characteristics coupled with a known or disclosed correlation between structure and function for the claimed genus of polypeptides.

The specification also fails to describe the claimed genus of a protein containing an amino acid sequence homologous to the amino acid sequence of SEQ ID NO:1 and having proliferation inhibitory activity on cancer cells or cell death inducing activity by the test set out in Lilly. The specification describes only two polypeptide species wherein it describes the polypeptide of SEQ ID NO:1 and one functional mutant of SEQ ID NO:1. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the claimed genus of protein containing an amino acid sequence homologous to the amino acid sequence of SEQ ID NO:1 and having proliferation inhibitory activity on cancer cells or cell death inducing activity.

8. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide having an amino acid sequence that is 95% homologous to the amino acid sequence of SEQ ID NO:1 and that contains amino acid residues 61-89 and 497-514 of SEQ ID NO:1 and that has a proliferation inhibitory activity on cancer cells or cell death inducing activity, does not reasonably provide enablement for a protein containing an amino acid sequence homologous to the amino acid sequence of SEQ ID NO:1 and having proliferation inhibitory activity on cancer or cell death inducing activity. The specification does not

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enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a protein having an amino acid sequence homologous to the amino acid sequence of SEQ ID NO:1 and having proliferation inhibitory activity on cancer cells or cell death inducing activity. This means the polypeptide may be any of a large number of polypeptides that has any degree of homology to the amino acid sequence of SEQ ID NO:1.

The specification teaches that the protein having the sequence of SEQ ID NO:1 had a cell-killing effect, particularly an apoptosis-inducing effect on human leukemia cells and a cell inhibitory effect on panel of human cancer cell lines (pages 23-29). The specification also teaches that a full-length protein of SEQ ID NO:1 having amino acids 1-524 and a mutant polypeptide having amino acids 1-514 exhibited apoptotic effect, whereas a mutant polypeptide having amino acids 1-496 did not exhibit a detectable

apoptotic effect (page 40, line 1 to page 41, line 3). The specification also teaches that it is understood that amino acids 497-514 of the sequence of SEQ ID NO:1 are essential to maintain the apoptotic effect of the protein (page 41, lines 4-6).

The teaching of the specification cannot be reasonably extrapolated to the scope of the claims because the claims are broadly drawn to any and all polypeptides that have any degree of homology SEQ ID NO:1 and applicant has not enabled all of these types of polypeptides because it has not been shown that these variant polypeptides are capable of functioning as that which is being disclosed and claimed. In particular, the specification teaches that only polypeptides having amino acids 497-514 of SEQ ID NO:1 will function as claimed.

Double Patenting

9. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

10. Claim 8 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 9 of copending Application No. 10/645094. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

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11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claim 8 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,291,644. Although the conflicting claims are not identical, they are not patentably distinct from each other because the cited claims of U.S. Patent No. 6,291,644 are directed species of the instant genus claim and thus makes obvious the genus.

13. The claims have been found to be free of the prior art. The closest prior art describes an isolated snake venom protein in (Raibekas et al., 1996, PNAS 93:7546-7551), which snake venom protein has cell death inducing activity and is 39% homologous to the protein of the instantly claimed SEQ ID NO:1 (Raibekas et al., 1998, Biochem. and Biophys. Res. Commun. 248:476-478). However, the prior art does not teach or suggest the invention of claim 8 because the specification indicates on page 9 that what is meant by the phrase in claim 8 of "a protein containing an amino acid sequence homologous to the amino acid sequence of SEQ ID NO:1" is a protein having not less than 70% homology to amino acid sequence of SEQ ID NO:1.

14. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine M. Joyce whose telephone number is 571-272-3321. The examiner can normally be reached on Monday thru Friday, 10:15 - 6:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Catherine Joyce
Examiner
Art Unit 1642



JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
11/14/05